“EFFICACY OF 3% HYPERTONIC SALINE NEBULISATION IN CHILDREN HOSPITALIZED WITH MODERATE BRONCHIOLITIS”

Dissertation submitted for

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CHENNAI

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INSTITUTE OF CHILD HEALTH AND

HOSPITAL FOR CHILDREN

MADRAS MEDICAL COLLEGE

CHENNAI

CERTIFICATE

This is to certify that the dissertation titled **"EFFICACY OF 3% HYPERTONIC SALINE NEBULISATION IN CHILDREN HOSPITALIZED WITH MODERATE BRONCHIOLITIS"** submitted by **Dr. R.RAJKUMAR.,** to the Faculty of Pediatrics, The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of M.D. Degree (Pediatrics) is a bonafide research work carried out by him under our direct supervision and guidance.

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DECLARATION

I **Dr. R. RAJKUMAR**, solemnly declare that the dissertation titled "**EFFICACY OF 3% HYPERTONIC SALINE NEBULISATION IN CHILDREN HOSPITALIZED WITH MODERATE BRONCHIOLITIS"** has been prepared by me.

This is submitted to the Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D.Degree Examination in Paediatrics.

Dr. R. RAJKUMAR.

Place : Chennai

Date :

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INSTITUTIONAL ETHICS COMMITTEE
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CERTIFICATE OF APPROVAL

To
Dr. R. Rajkumar
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Dear Dr. R. Rajkumar

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Efficacy of 3% hypertonic saline nebulisation in children hospitalized with moderate bronchiolitis randomized control trail" No.10042012.

The following members of Ethics Committee were present in the meeting held on 19.04.2012 conducted at Madras Medical College, Chennai -3.

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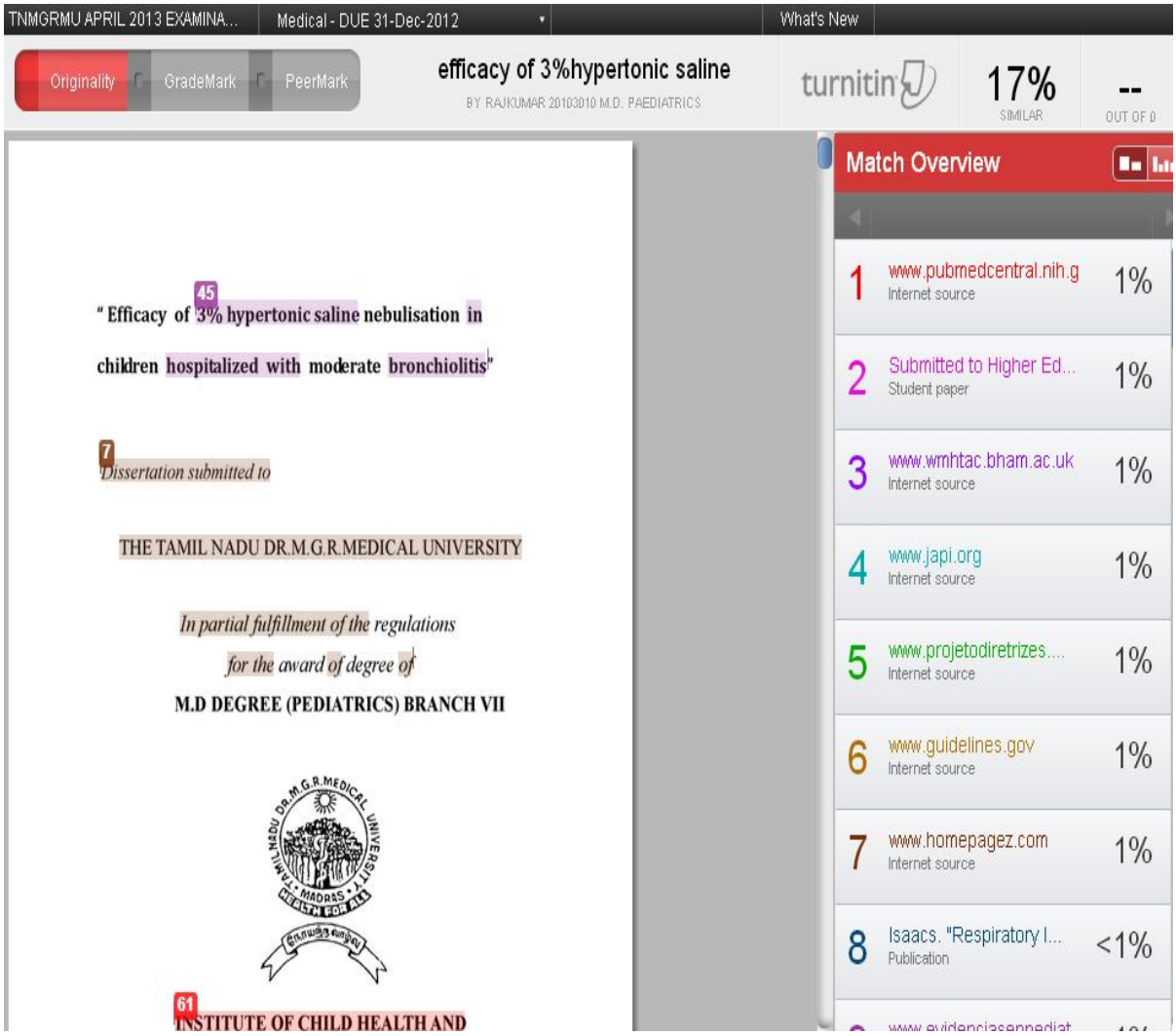
We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee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In partial fulfillment of the regulations
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CONTENTS

I. INTRODUCTION

Bronchiolitis is one of the common causes of lower respiratory tract infections in infants and young children.Bronchiolitis is a predominantly viral disease .The virus which is implicated for more than 50% of cases is the respiratory syncytial virus.Other etiological agents which are implicated in bronchiolitis include parainfluenza, adenovirus and mycoplasma.Other new pathogens which are implicated include human boca virus, and the human metapneumovirus.

The human Bocavirus can occur as a coinfection with respiratory syncytial virus. Bronchiolitis mainly occurs during august through november which coincides with respiratory syncytial virus season.The period of infectivity in cases of respiratory syncytial virus is 3 days before to 21 days after onset of symptoms.

There are host factors too which have to be considered in case of bronchiolitis.For example bronchiolitis is more commoner in boys than girls.It is more in infants who are deprived of breast milk.It is also more common in overcrowded conditions.The prevalence of bronchiolitis is more in cases of mothers who smoke during

pregnancy.Younger mothers too have a higher risk of having a child with bronchiolitis.

The clinical manifestation of bronchiolitis is more severe in young infants as they poorly tolerate bronchiolar edema compared to adults.The immunity of the host too plays a significant role in deciding the severity of clinical manifestations.The nature of the virus too plays a role.

There will be severe clinical manifestations if there are pre-existing smaller airways and diminished lung function.Innate immunity plays a significant role in the pathogenesis of bronchiolitis.The cytotoxic damage caused by the eosinophil cationioc protein also has a role to play in the pathogenesis of bronchiolitis.Interleukins and tumor necrosis factor may be differentially expressed depending on the different types of inciting agents.If the inciting agent is more than one, that too will affect the varied manifestation of bronchiolitis.

Acute bronchiolitis is due to bronchiolar obstruction which is caused by airway edema,mucus collection and cellular debris.Minimal

bronchiolar wall thickening will also lead to significant air way obstruction because of the inverse relationship between the bronchiolar wall and its radius.Resistance in the bronchioles is more during inspiration as well as expiration but as the radius is very much decreased during expiration there is more and more air trapping in cases of bronchiolitis.

If the obstruction progresses there will be air trapping leading on to development of the atelectasis.Hypoxia and hypercapnia develop subsequent to the disease process.

The diagnosis of bronchiolitis is mainly a clinical one. Bronchiolitis is mainly diagnosed by a constellation of symptoms and signs . Depending on the severity of clinical manifestations Indian academy of pediatrics has classified bronchiolitis in to mild, moderate and severe disease.

In cases of mild bronchiolitis the infant will have a normal ability to feed and the oxygen saturation will be more than ninety two percent.

In cases of moderate bronchiolitis the infant will have shortness of breath during feeding,moderate distress with some chest wall retractions and nasal flare will also be there.The oxygen saturation will be less than ninety two percent which is correctable by oxygen.

In cases of severe cases of bronchiolitis there will be reluctance to feed or inability to feed .Severe distress with marked chest wall retractions and nasal flare as well as grunting will be there.The saturation of oxygen will be less than ninety two percent and it may or may not be correctable with oxygen therapy.

While diagnosing bronchiolitis other conditions in infants and young children which present with wheeze must be kept in mind.Asthma and allergy present in similar manner and viral bronchopneumonia when it presents with wheeze is almost clinically indistinguishable from bronchiolitis.

Foreignbody aspiration too is a common cause of wheeze.Other congenital airway anomalies like laryngotracheomalacia have to be kept in mind before making a diagnosis of bronchiolitis.Gastro esophageal reflux too causes wheeze by virtue of it producing vagal or

neural reflex which will increase airway reactivity and and also airway resistance.

Other chronic causes of wheeze like cystic fibrosis has to be kept in mind.Investigational modalities like x ray are mainly used to exclude other diagnosis.In bronchiolitis there will be hyperinflation which will also be present in cases of viral bronchopneumonia.

Blood investigations are not routinely performed and they only play a role if there is bacterial super added infection.Blood cultures too don't have a routine role in cases of bronchiolitis.

The treatment modality in cases of bronchiolitis is largely supportive.Mild cases of bronchiolitis can be safely managed at home .Even amongst moderate bronchiolitis only children whose saturation is below par require inhospital admission and treatment.Severe cases require intensive care.

Trial of bronchodilators are used in the setting of a clinical response after a trial nebulization.If there is no response after 24 hrs they are not continued.Intravenous fluids have to be used only if there

is significant respiratory distress which prevents oral feeds.Nasogastric feeds can also tried.

IV fluids does not provide any significant advantage over nasogastric feeds.There have been numerous studies investigating the various agents used in the treatment of bronchiolitis.None of the tried treatments have been proven to significantly alter the course of disease. 3% hypertonic saline too has been tried in bronchiolitis and found to alter the duration of the disease and clinical severity in some studies.

Since the main treatment of bronchiolitis is mainly supportive we decided to work on the morbidity part and also to find out if there is any significant difference in the length of stay.

Since no broncodilator has a proven benefit in cases of bronchiolitis we decided to try nebulised hypertonic saline alone without any bronchodilator or epinephrine.And also not many studies have been conducted in the Indian context which in many ways are quite different from the American or European context when we take in to account the environmental,nutritional,immunological as well as

the genetic makeup of our population.And also this seemed to be a cheap and practically feasible in a developing country like India

REVIEW OF LITERATURE

Definition:

Bronchiolitis is defined as per American academy of pediatrics definition as a constellation of clinical symptoms and signs like rhinorrhoea, cough, wheezing ,tachypnoea ,and increased respiratory effort manifested as grunting, nasal flaring and intercostal and or subcostal retractions in children less than 2 years of age.

Moderate bronchiolitis is characterized by feeding difficulty,moderate respiratory distress with some chest wall retractions and nasal flaring and oxygen saturation less than 92% which is correctable with oxygen.As bronchiolitis is mainly diagnosed clinically there is considerable difference amongst clinicians in its diagnosis.

There seems to exist a confusion world over regarding the diagnostic criteria which have to be used in diagnosis of bronchiolitis.Some studies have used tachypnoea and some have used wheezing and some have used nasal flare in diagnosis or inclusion criteria[1].

The north Carolina group includes expiratory wheeze in the presence or absence of increased respiratory rate, substernal retractions along with the feature of air trapping[2].

In United kingdom the diagnosis of bronchiolitis is even more confined.It is regarded as a seasonal acute lower respiratory tract infection which manifests with coryza in the first two to three days then, develops the lower respiratory symptoms.Wheeze associated lower respiratory tract infection is also a terminology used .Viruses can cause wheeze in bronchial asthma ,viral bronchopneumonias and the different outcomes with various treatment modalities can be attributed to this[3].

EPIDEMIOLOGY:

The major fraction present with upper respiratory tract manifestations and at about forty percent present with lower respiratory tract manifestations.Around one to two percent require inpatient care out of which five to ten percent of patients require artificial respiration[4].The morbidity of bronchiolitis incurs a considerable health expenditure on the nation as well as the

individual.And repeated episodes of wheezing too occur in case of bronchiolitis producing significant functional impairment affecting the quality of life of the individual[4].

ETIOLOGY:

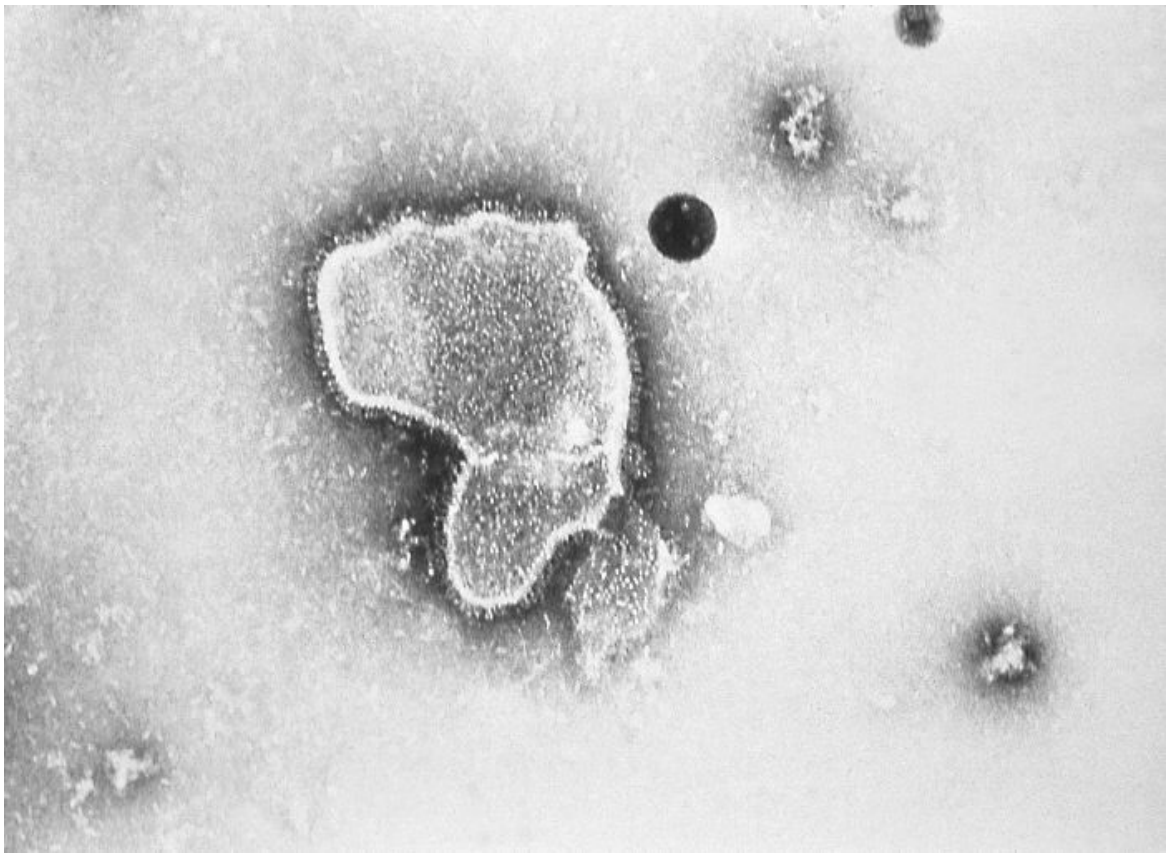
Apart from respiratory syncytial virus, parainfluenza, human boca virus, human metapneumovirus the human corona virus is also implicated in the etiology of bronchiolitis.Respiratory syncytial virus is an enveloped rna virus.It comprises of a single stranded negative sense genome and multiplication takes place inside the cytosol of a cell.The virus is not known to undergo antigenic shift, hence reassortment of virions cannot happen which happens in the case of influenza virus.It comes under paramyxoviridae family accompanied by parainfluenza and measles virus.It belongs to the pneumovirinae group which also encompasses human metapneumovirus.

Two antigenic subtypes of respiratory syncytial virus are there which differs by virtue of their surface proteins.The reinfections causing recurrent bronchiolitis is attributed to the point mutations which take place with the viral ribonucleic acid polymerase.

Respiratory syncytial virus multiplies in cell lines such as the Hela or the Hep-2 cell lines leading to the characteristic formation of syncytium from which the virus derives its name from.It is not known whether the syncytium formation occurs in vitro alone or it occurs in the invivo setting too.

Kneyber et al[6] showed that there is no significant difference between the two types of respiratory syncytial viruses which were compared.No difference was seen in the duration of stay and the need for oxygen as well as the need for intensive care. Zambon et al[5] studied the phylogenetics of the RSV over a period of three seasons and came to the conclusion that they cause the same spectrum of manifestations involving the upper as well as lower respiratory tracts and caused disease both in children young infants as well as adults alike.

Respiratory syncytial virus causes disease in all age groups.Infection is universal by the time children atttain two years of age.The manifestations in case of RSV is very much similar to the influenza virus hence differentiating between these two etiologies is quite cumbersome.However the systemic prodrome features will be there in cases of influenza infections.



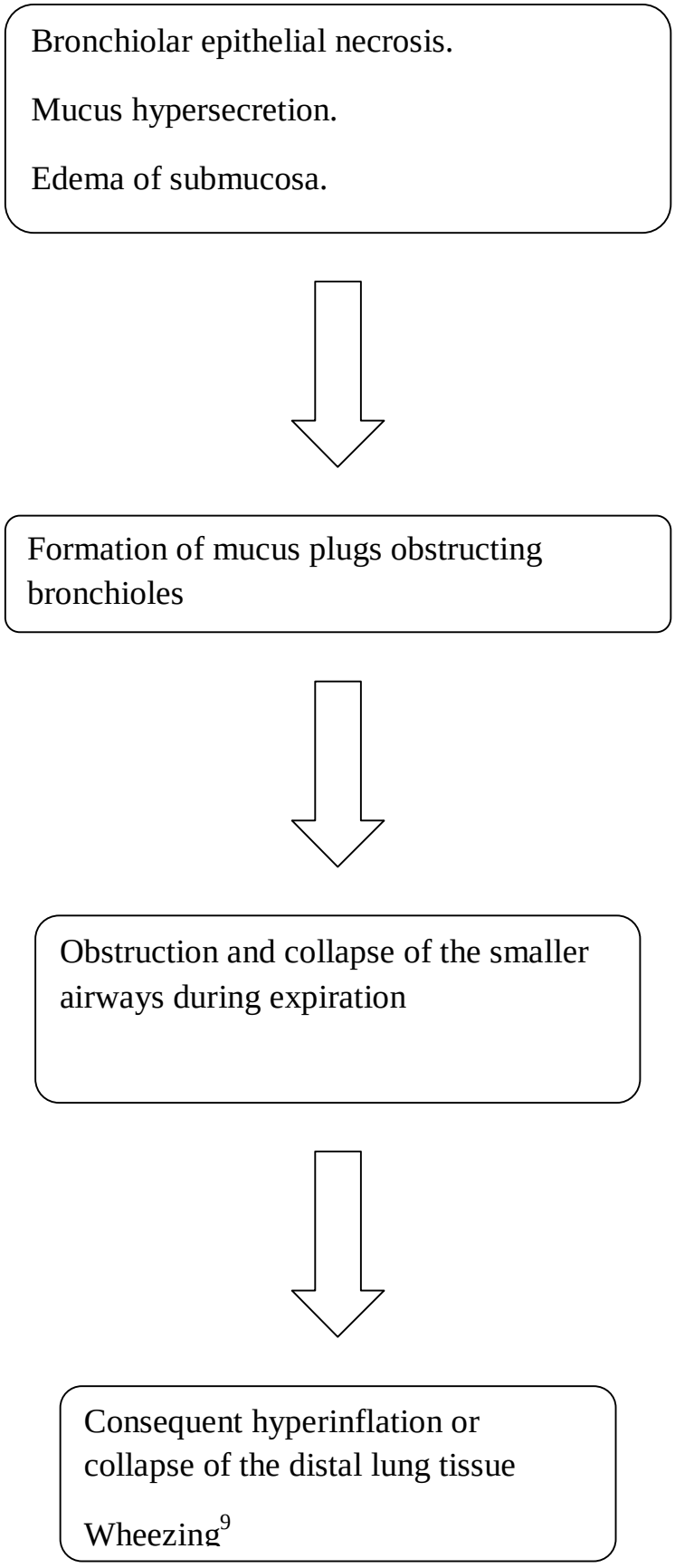
ELECTRON MICROSCOPY PICTURE OF RESPIRATORY SYNCYTIAL VIRUS SHOWING THE CHARACTERISTIC SYNCYTIUM FORMATION.

Human metapneumovirus is a enveloped single strand nonsegmented negative sense ribonucleic acid virus.The human metapneumovirus is closely related to avian pneumoviruses .The decreased pathogenicity of the metapneumoviruses compared to the wild type respiratory syncytial virus is attributed to the difference of structural proteins in case of metapneumovirus[7].

The human metapneumovirus outbreaks coincide with the second half of the respiratory syncytial virus season.But infections do occur through out the year sporadically.Infection is known to occur by virtue of close contact or by aerosolized spread through droplets.

Nosocomial infections have been reported and isolation of the contacts as well as proper hand washing of medical personnel are advised.The virus affects individuals with reactive airway disease in a more severe manner. Hcov-63 has been isolated from a seven month old child with conjuctival infection and bronchiolitis[8].Later it was isolated from several clinical specimens .

PATHOGENESIS:



The airway of young infants typically do not react in a hyper responsive manner .Host factors too play a role .The immune response itself sometimes affects the host in a detrimental manner.And there is evidence to suggest the role of genetic factors also in the severity of the disease.

The severity of Respiratory syncytial virus infection is more in the case of immunocompetent host compared to a immune compromised host.Children who received formalin inactivated RSV vaccine experienced more severe symptoms after getting infected by wild type of RSV subsequently. Many children died after RSV infection postvaccination.This impeded the development of newer vaccines for RSV infections.RSV symptoms are more severe when the viral multiplication is waning, once more implicating immunity in the pathogenesis of RSV infections.

Several immunological processes are doubted to play a role in respiratory syncytial virus infections.The occurrence of bronchiolitis after the primary infection caused by respiratory syncytial virus , the development of recurrent wheezing are all due to a complex interplay of various agent and host interactions.

T-LYMPHOCYTES AND ANTIGEN PRESENTING CELLS :

An immunological response is mounted by the host against the agent so as to eradicate it from the respiratory tract.Respiratory syncytial virus specific cluster of differentiation four and eight cells are produced.

If there is insufficient immune response against the virus the virus will persist for a longer period.Respiratory syncytial virus continues to be shed from the respiratory tract for a duration of around nine days in pediatric age group younger than one year of age. High levels of the virus might be there in secretions even though clinical resolution would have occurred by that time.

In HIV affected individuals the virus is shed for a duration of around 30 days. When animals were inoculated with specific T-lymphocytes in addition to the clinical improvement that happened, there was inflammation mediated by these T-lymphocytes thus providing the insight, that they do play a very important role in the pathogenesis of the disease. They contributed to the hyper responsiveness of the air way.These experiments prove that inspite of

the role of an effective immune response which helps in clearing the infection they also play a role in causing airway injury.

In murine studies it has been demonstrated that CD-4 T lymphocytes which mount an immune response against the fusion protein provides the necessary protection against the disease .This is accomplished with the help of cytotoxic CD-8 lymphocytes, and also with the help of antibody of the igG type.

Circulating antibodies of the immunoglobulin G class are produced several days after the development of infection. These are primarily directed against the fusion proteins of respiratory syncytial virus. The proposition that higher levels of antibodies proved detrimental has been proven to be wrong after its beneficial effects were observed in the newborns due to the transfer of antibodies through the breast milk. And also it was shown that after a first attack of the bronchiolitis,the subsequent attacks were of lesser severity mainly attributable due the primary immunity acquired after the infection.

CD-4 lymphocytes direct against the g-protein leads to the helper cell mediated immune response leading on to the production

of interleukins 5 and 10 and a eosinophil influx[11]. These interleukins are thought to be responsible for the hyperresponsiveness which is observed. If respiratory syncytial disease is mediated by helper T cells , then there must have been an association with allergic component, which has not been proven.

Lot of cohort studies have been done, but they have failed to establish any association between respiratory syncytial virus and allergic component[12].A study by sigurs et al[13] has come out saying that respiratory syncytial virius infection leads to sensitization against allergens in the air as well as later manifestation of allergy.

The natural immunity too plays a role in protection through eosinophils, polymorphs and APC'S. Neutrophil degranulation leads to release of substrates which can be easily detected and there is a relation between the levels of released substrates and disease severity. The mucosa is protected by migration of monocytes as well as dendritic cells. These cells might lead on to the development of airway hyper responsiveness or they might delay the T cell mediated immune response.

ROLE OF DUAL INFECTIONS:

Hament et al[14] has proved that a respiratory syncytial virus infected respiratory epithelium is easily infected by pneumococcal virus. This was shown to be due to the increased binding. And a co-infection also leads to a much stronger binding to the respiratory epithelium. The effect was related to the dose as well as the different strains causing the infection.

This was supported further by a study from south Africa[15] showing the association of pneumococci with the respiratory syncytial virus associated pneumonia.

Semple et al[16] demonstrated that a dual infection with human metapneumovirus and respiratory syncytial virus leads to a severe disease. The presence of co-infection was found to be seventy two percent in a intensive setting amongst bronchiolitis cases compared to ten percent in a general ward.

ROLE OF GENETICS:

The genetic component plays a role in affecting the outcome of the disease process. This is due to the polymorphisms in the genetic components requisite to mount an effective immune response. The genetic difference also plays a role in determining the severity of the disease.

Lofgren et al[17] provided an insight to the polymorphisms in surfactant proteins and respiratory syncytial virus infection. A certain haplotype was shown to produce a more severe disease that is 6A2/1A3C .

A difference in polymorphisms of innate immunity too plays a role in shaping the course of the disease. Venter et al[18] and Bleek et al[19] showed the difference in the reaction of T lymphocytes to the epitopes G, N and F.

This despite the fact that the epitopes are largely preserved in wild type of respiratory syncytial virus. Venter et al[18] showed a interferon gamma response in twenty one out of thirty eight individuals when challenged with over lapped peptides. This was

found to be due to a HLA B8 which was a restricted epitope. Van bleek et al[19] showed a significant inter individual variation in the interferon gamma production . This was decided by the extent to which the epitopes were recognized.

Tal et al[20] studied the polymorphisms in TLR-4 which were shown to produce a more severe respiratory syncytial virus disease. Severe cases were defined by the need for in hospital and intensive care. They were compared with mild bronchiolitis and a group of healthy adult population.

Hull et al[21] showed that interleukin eight 251 A polymorphic variations in the genes coding for interleukin eight had a increased prevalence in patients with severe degrees of respiratory syncytial virus disease. And also this polymorphic variation was shown to be associated with the chronic effects of respiratory syncytial virus-bronchiolitis.

Hoe bee et al[22] studied the polymorphisms in interleukin-four ,interleukin-4-R, and interleukin ten. They showed that a polymorphism in IL-4 which is a thymidine substitute for cytosine

leads on to increase in hospital admissions in case of RSV infections. And the association was stronger in babies more than six months of age. The interleukin 4Ra-R551 genetic polymorphisms was present in more severe manner in babies more than six months of age.

Similar results was shown by choi et al[23] amongst Korean population. Hoebee et al[22] highlighted that patients homozygous for interleukin ten 592 c or interleukin ten 592a could have a clinically severe bronchiolitis when compared with a population which is heterozygous for the same.

Wilson et al[24] showed a relationship between genetic polymorphisms invoving interleukin ten and the increasing need for artificial respiration. This homo-heterozygous variation has not been studied before.

Hull et al[25] studied the genetic polymorphisms involving the interleukin-5 receptor which was said to produce severe bronchiolitis.This receptor interacts with MIP 1-A. And it is known to produce a vital role in pathway of bronchiolitis.

AGE AND BRONCHIOLITIS:

Younger the chid more severe is the clinical presentation of bronchiolitis especially in infants less tnan six months. Bont et al[26] studied the correlation of post gestational age less than forty four with the severity of manifestation of the illness. It's quite possible that younger chidren fail to produce a effective immunological response by virtue of interferon gamma production thus leading on to a clinically severe disease disease compared to older children.

Culley et al[27] studied in murine models the effect of respiratory syncytial virus at two week intervals thus stressing the impotant role the age plays in the pathogenesis of bronchiolitis. Murine models at younger age developed a more severe bronchiolitis due to ineffective interferon gamma release , instead interleukin four predominates leading to hyper reactive response.

Murine models infected at more advanced gestational age showed a stronger interferon gamma release compared to younger ages. But the production of interleukin four was more muted. These

studies showed the important role that interferon gamma release plays as gestational age advances.

BRONCHIOLITIS AND REACTIVE AIRWAY DISEASE:

Several works have shown the association between bronchiolitis and later development of reactive airway disease. Episodic wheeze which follows bronchiolitis develops in forty two to seventy one percent of patients, and it occurs mainly in less than two year old age group[28]. Recent studies have shown that repeated wheeze following the disease decreases as the child ages, but this might be different in patients who have atopy and in those who do not have atopy.

PATHOLOGY OF BRONCHIAL HYPER-REACTIVITY AFTER RSV DISEASE:

Studies have shown the role of T lymphocytes -2 in the hyper responsiveness following the disease. In animal models neurotropin growth factor has been shown to play a role in hyper responsiveness following a episode of the disease. Piedemont et al showed a link

between neural stimulation and vascular leakage which is present even after the initial phase of the disease.

Piedemont et al hypothesized that a remodelled airway results following an attack of respiratory syncytial virus disease. Animal models have shown the persistence of respiratory syncytial virus in the lung despite active t-lymphocyte response.

Such persistence of RSV leads to the development of susceptibility to other infections. It could also lead to development of atopy. No definite link has been established between bronchiolitis and bronchial asthma at later ages.

CLINICAL MANIFESTATIONS:

Almost all less than two years of age get infected with respiratory syncytial virus. Fifty percent of the patients get clinically significant disease and amongst them a few require in hospital care. The disease starts with running nose, fast breathing, breathlessness intercostal and subcostal retractions along with wheeze.

There will be decreased oxygen saturation and the chest X-ray might reveal bilateral diffuse hyperinflation of lungs , flattening of diaphragm , prominence of retrosternal space and bulging of intercostals spaces. Patchy or peribronchial infiltrates suggestive of interstitial pneumonia occur in the majority of infants.

Atelectasis is observed in most infants but consolidation is observed in only twenty four percent of patients.

Minimal pleural fluid can also be present. Thirteen percent of infants with illness severe enough to require hospitalization have normal chest roengenograms.

In general only infants more than one month develop syndrome of bronchiolitis. In urban settings the peak age is two months but in rural settings it's a bit later. Antigenic studies shall be performed in epithelim for the detection of the virus. Direct immunofluorocence is used for the same.

There are certain settings where the manifestations will be severe. When more than one of these settings is present the manifestation or outcome is more severe accordingly .

RISK FACTORS FOR CLINICAL DETERIORATION IN BRONCHIOLITIS[30]

Presenting features	Fast breathing ,decreased oxygen saturation and refusal of feeds or inadequate hydration
Younger age	Less than 1 year of age
Coexisting illnesses	Chronic lung disease, heart diseases , and cystic fibrosis as well as immunodeficient states
Preterms	Gestation less than thirty six week
Other factors	Poverty, overcrowding, smokers in the family, hereditary factors

Environment does play a role in modifying the manifestation of the disease. Carbonel estrany et al[31] did a follow up study in preterm's less than thirty two weeks of gestation and identified the additional factors. Inpatients who were admitted were prognosticated using these factors – a lesser number of gestational days, age less than three months and exposure to second hand smoking . Similar

results were arrived too using infants of gestational age thirty three to thirty five weeks.

Overcrowding, exclusive breast feeds given for less than two months, wheeze in the family were identified as risk factors for inpatient admission in the previous study. Law et al did a follow up study in Canada and identified similar factors as a risk. Boys were found to have a higher risk for needing inpatient care.

It is pretty clear from these studies that the environment and population characteristics play a role in the need for inpatient care. The environment and the genes also play a role in deciding the severity of the disease.

Second hand smoking too carries an increasing risk of inpatient care. Inpatient care for the disease has been on the rise primarily because of the better prognosis of patients with other comorbidities. And also the increasing use of pulse oximetry as a clinical tool too has played a role in identifying hypoxia and grading the severity of the disease.

CLINICAL FEATURES:

Bronchiolitis is more from august to december but it can occur at any time of the year . A h/o contact with patients with a cold prodrome is often elicited. Initially there will be a running nose , cough and refusal of feeds. Fever grade is decided by the infecting agent.

Most patients have fever at the time of clinical presentation. Patients with influenza or parainfluenza as a cause have higher grades of fever. Severity can be mild, moderate or severe as graded by IAP. Children might present with cyanosis in cases of respiratory failure[30]. Physical examination in cases of bronchiolitis will reveal wheeze, crepitations as well as prolongation of the expiratory cycle.

Other signs can be conjuctival inflammation, acute otitis media as well as rhinorrhoea.There can be abdominal distention due do hyperinflated lungs.

RESPIRATORY DISTRESS ASSESSMENT INSTRUMENT:

Table 1. Wheezing and Retraction Scales for the Respiratory Distress Assessment Instrument (RDAI).*

Symptom	Points					
	0	1	2	3	4	Maximum
Wheezing						
During expiration	None	End	First half	First three quarters	Throughout	4
During inspiration	None	Part	Throughout	—	—	2
No. of involved lung fields	0	1 or 2	3 or 4	—	—	2
Retractions						
Supraclavicular	None	Mild	Moderate	Marked	—	3
Intercostal	None	Mild	Moderate	Marked	—	3
Subcostal	None	Mild	Moderate	Marked	—	3
Total						17

* Both wheezing and retractions were scored. The total score on the RDAI is the sum of the scores for each row, with a range of 0 to 17; higher scores indicate more severe disease.

The RDAI is used to grade severity in cases of bronchiolitis. The tool is also used to observe response to treatment. The highest score given is seventeen and the lowest score is zero. Higher the score more severe is the level of respiratory distress.(LOWELL ET AL 1987)[33].

Similarly Wang et al[34] have come out with a score based on wheeze, retractions and general clinical condition. The score ranges

from zero to twelve. Grading of severity –For mild it should be zero to four, moderate four to eight, and for severe it should be more than nine.

INVESTIGATIONAL MODALITIES IN BRONCHIOLITIS:

It is mainly a clinical one. They are undertaken to exclude alternative causes of respiratory distress in young children. A mild degree of increase in leucocyte count with a normal DC is seen in cases of bronchiolitis. Hypoxemia is made out by oxygen saturation or by means of bllood gas analysis. Hypercapnoea might be there in severe cases of bronchiolitis. Viral detection is by indirect fluorescent antibody technique, polymerase chain reaction, RIA or by cultures. Viral detection might prevent unwarranted use of antimicrobials.

THERAPY AND PREVENTIVE ASPECTS:

There is no gold standard treatment in the case of bronchiolitis. It is mainly supportive in nature. There is no indication for the pharmaceutic agents used in the management of bronchiolitis.

With the advances in modern medicine it is increasingly becoming clear that there is minimal role for therapeutic agents and health education is being targeted at doctors to make them aware of these facts.

Most patients can be home managed after educating the parents regarding the danger signs as well as giving nutritional advice. The need for inpatient care is determined by the age of the child as well as need for IV fluids , the severity grading and other socio-economic factors.

The therapy of children with bronchiolitis is mainly by means of humidified oxygen , maintaining adequate hydration orally or by intravenous fluids and restricting the handling of the child. The oxygen saturation must be maintained more than ninety two percent . Chest physiotherapy is found to be ineffective in the management of bronchiolitis[35].

Numerous therapeutic agents are tried in the therapy of bronchiolitis. There is no rationality in the routine use of bronchodilators unless there is a history of asthma. But most

clinicians give a trial of bronchodialators even though there is no robust evidence in its use in cases of bronchiolitis.

The obstruction which is there in cases of bronchiolitis is mainly by means of cellular debris as well as mucus, bronchoconstriction plays a very minimal role. Moreover the use of beta adrenergic bronchodilators have been studied in detail and found to have a very minimal role. There is only a temporary improvement in clinical use of these agents and the benefits have to be weighed against the various disadvantages that they have, including the cost of these agents.

Adrenaline nebulisation is widely used in the treatment of bronchiolitis . It mainly acts via the alpha adrenergic receptors thereby decreasing the air way edema which is present in cases of bronchiolitis. It decreases airway edema by means of its vasoconstrictive effect. However a review of eight RCT'S regarding adrenaline nebulisation concluded that there is no significant advantage with its use. It was found to have only a short term benefit eventhough it was found to be more effective than salbutamol as well as placebos[37].

Regarding the role of corticosteroids meta-analysis was done and it was found that it doesn't impact the duration of in hospital stay nor was it found to modify the severity of the disease[38]. There is no recent evidence of steroids as a treatment modality in cases of bronchiolitis. Irrespective of the route of administration of drugs steroids are found to be in effective in cases of bronchiolitis.

This is applicable to children presenting in the ED as well as those requiring inhospital care. Its role in the setting of bronchopulmonary dysplasia is controversial.

Children deteriorating might have a ineffective immune system or they might have other risk factors which play a role in pathogenesis of the disease. The modality showing some promise in treating critically ill cases of bronchiolitis is the use of surfactant in the setting of secondary surfactant inactivation.

3 RCT'S have been done with surfactants but they weren't comparable due to lack of uniformity in ventilation strategy and a meta analysis came to the conclusion that they were found to have a non significant decrease in inhospital stay.

ROLE OF ANTIVIRAL AGENTS:

Ribavirin an antiviral agent administered by aerosolized route has been used for infants with congenital heart disease or chronic lung disease. It is delivered as a small particle aerosol for 18 -20 hrs a day.There is no convincing evidence of a positive impact on clinically important outcomes such as mortality and duration of hospitalization. Likewise there is no support for RSV immunoglobulin administration in previously healthy children.

However reduction of severity is possible through administration of pooled hyper immune RSV intravenous immunoglobulin.

Other agents which are used include immunoglobulin, a mixture of helium and air[39], erythropoietin[40] and nitric oxide[41] . But none of the agents were found to offer benefit in the treatment of bronchiolitis.

Recently the therapy which is increasingly being tried in the management of bronchiolitis is the Hypertonic saline nebulisation. Hypertonic saline nebulisation has been shown to increase the

mucociliary transport rates in conditions like cystic fibrosis as well as in reactive airway disease. Hypertonic saline nebulisation has been tried more and more in cases of bronchiolitis (sarell 2002[42] ; mandelberg 2003[43] ; Taal[44] 2006; and kuzik[45] 2007) . The way by which hypertonic saline offers benefit in bronchiolitis is as follows

1. Hypertonic saline removes the ionic bonds as well as it decreases the cross links in the mucus. Thereby it improves the mucus rheological property. It decreases the viscosity of the mucus.

2. Hypertonic saline causes osmosis of water in to mucus thereby improving the mucus rheological property. 3 . Hypertonic saline decreases the airway oedema in bronchiolitis(Mandelburg[43] 2003; sarrell[42] 2002). Hypertonic saline increases the motility of the cilia.

3. Hypertonic saline also induces the sputum formation and coughing which leads to increased clearance thus relieving the airway obstruction(Mandelberg[43] 2003) . These are various theories put forward favouring the use of hypertonic saline nebulisation in cases of bronchiolitis.

Recent studies from the west have shown benefit in cases of bronchiolitis with the hypertonic saline nebulisation both in OPD as well as in inpatients. Mandelberg et al showed that in moderately ill children hospitalized with bronchiolitis three percent hypertonic saline/ 1.5mg adrenaline[43] decreases the severity as well as it decreases the duration of stay when it was compared with 0.9 n saline along with 1.5mg adrenaline.

Sarell et al showed that in moderately ill cases of bronchiolitis treated as op, 3% hypertonic saline along with 5 mg terbutaline was found to be beneficial in decreasing the symptomatology when compared to 0.9 n saline alongside 5 mg terbutaline[42].

Kuzic et al came to the conclusion that three percent hypertonic saline nebulisation is a safe, cost effective and effective treatment modality in cases of moderately severe bronchiolitis[45].

IS IT SAFE TO USE?

Studies have come out saying that a concentration of more than seven percent causes bronchospasm[46] in cystic fibrosis patients. The use of a lesser concentration of hypertonic saline circumvented

this problem and also the concomitant use of a bronchodilator has alleviated the problem.

PREVENTIVE ASPECTS:

Prevention ranges from the use of IV immune globulin to the use of respiratory syncytial virus specific polyclonal hyper immune gamma globulin ,to the use of murine derived humanized monoclonal antibody palivizumab.

Hyper immune globulin was never popular because of long time taken to administer it and also the risk of infection as well as its interfering with vaccines which are live attenuated.

In randomized control studies palivizumab administration at a dose of 15 mg per kg decreased the duration of in hospital stay. It was administered over a five month period. It decreased the inhospital stay in preterms by fifty five percent and forty five percent in case of congenital heart diseases which were hemodynamically significant. Palivizumab did not provide any advantage with regard to mortality.

Palivizumab has become the drug of choice in prophylaxis of respiratory syncytial virus bronchiolitis in children more prone to the disease. The AAP recommends palivizumab prophylaxis in cases of bronchopulmonary dysplasias as well as in infants having heart defects and also in preterms less than thirty five weeks gestation[47].

One dose per month is given for 5 months duration. The dose is 15 mg /kg given intramuscularly. These recommendations are difficult to practice in a country like ours especially considering the exorbitant cost of the drug. The number of children requiring RSV prophylaxis as per AAP recommendations is quite less. The option is not considered as cost effective.

Some countries restrict palivizumab use to infants with bronchopulmonary dysplasia especially during the peak season. Despite advances in science due to the complex nature of the agent there is no breakthrough in vaccine research. Studies came to a standstill when respiratory syncytial virus vaccines produced disease in the vaccinees accidentally.

Drugs which interfere with the viral replication are being investigated and they might one day provide the necessary break through.

CONCLUSION

It is quite clear that there being no gold standard management strategy in bronchiolitis, the management is largely supportive. Because of the prevailing confusion in treatment strategies several agents are doing the rounds. And there is no role for bronchodilators, corticosteroids or epinephrine nebulisation in a routine manner. In this setting hypertonic saline nebulisation can be safe and effective in the management of bronchiolitis. Several studies have been done in the west and the results are quite positive. Hypertonic saline if proven to be effective could have beneficial clinical implications.

OBJECTIVES

To establish the efficacy of nebulized hypertonic saline without Bronchodilators in reducing respiratory distress, thereby, clinical severity in cases of moderate bronchiolitis.

STUDY JUSTIFICATION

Since the main management of bronchiolitis is largely supportive , we would like to work to reduce the respiratory distress , thereby , the clinical severity by means of hypertonic saline nebulization alone without bronchodilators or epinephrine.

And this modality of treatment is affordable and practically feasible in a developing country like ours.

And also not many studies have been conducted in the Indian context which in many ways is quite different from the European or American context.

METHODOLOGY

Study design:

Interventional study, Randomised control trial

Study group:

Children receiving 3 % hypertonic saline along with supportive therapy.

Control group:

Children receiving supportive therapy alone.

Study period:

Protocol preparation-Dec 2010-feb 2011

Sample Size : 116

Data collection:

March 2011-august 2012

Data analysis and manuscript preparation:

Sep 2012 - Nov- 2012

Submission of report:

December -2012

DEFINITIONS

Case definition:

Bronchiolitis is defined as per American academy of pediatrics definition as a constellation of clinical symptoms and signs like rhinorrhoea, cough , wheezing , tachypnoea , and increased respiratory effort manifested as grunting , nasal flaring and intercostals and or subcostal retractions in children less than two years of age.

Moderate bronchiolitis is characterized by , feeding difficulty, moderate respiratory distress with some chest wall retractions and nasal flaring and oxygen saturation less than 92 % which is correctable with oxygen.

Respiratory distress was defined by intercostal, subcostal or supra sternal retractions.

Child considered to be tachypnoeic-Based on World health organization guidelines.

1. 60 per minute in age less than two months.
2. 50 per minute in age two to twelve months.
3. 40 per minute in age more than one year.

Inclusion criteria:

Hospitalised children in a tertiary care hospital in Chennai with a clinical diagnosis of moderate bronchiolitis.

Exclusion criteria:

- Presence of complicating underlying illnesses.
- Bronchopulmonary dysplasia or chronic lung disease.
- Neuromuscular impairment.
- Congenital heart disease.
- Treatment with corticosteroids
- Previous episode of Wheeze

Children who met the inclusion criteria were recruited for the study. Hundred chidren enrolled according to the desired sample size.

Written consent was documented from all the parents before enrolling them in to study.

Ethical committee approval was obtained from the institutional ethics committee.

Conflict of interest: Nil

Financial support: Nil

Patients were randomized in to two groups based on computer generated random numbers.

The eligible children who were recruited were randomized in to two groups using random table in blocks of ten.

Study group received 3% hypertonic saline nebulisation 3 ml 8^{th} hourly in addition to supportive therapy . The nebulisations were continued till discharge.

Children in control group received supportive therapy alone.

Nebulisations were administered using nebulisation chambers which are routinely available in our wards. The nebulisations were administered along with humidified oxygen. Humidified oxygen was given at a rate of six litres per minute.

Children were admitted to the study within twenty four hours of admission. The history was obtained from the mother and the chidren were examined at the time of entering in to the study as well as everyday. Vital signs were recorded in all the patients. Children were observed for cyanosis , retractions as well as anemia.

Detailed examination of the respiratory system was also done. A complete blood count and a x ray chest was done for all the children. All the children were given oxygen and IV fluids were administered for children who did not tolerate oral feeds.

Length of stay in the hospital was taken as the primary outcome.

Cough resolution time and wheeze resolution time were taken as secondary outcomes in the study.

Adverse effects were recorded for the study group.

The length of stay was recorded using a previously validated method. Every day the patients were examined for four conditions for which they were retained in the study.

1. Child on drugs for the disease.
2. Child administered humidified o2 or IVF because of the disease.
3. Children retained because of co- morbid conditions.
4. Children who could not be sent home because of conditions at their home.

Hospital days were recorded only when the reason was administration of drugs or humidified o2 administration.

Time of discharge will be decided by the treating consultant.

Criteria for discharge:

1. Afebrile and no clinical signs of clinical respiratory distress .
2. Spo2 should be more than ninety six percent and the child should be comfortable in room air.
3. Feeding should be possible orally.

Statistical method:

All data entered in data collection form are entered in excel spread sheet. Descriptive statistical analysis was done in the study.Continuous measurement is represented by mean plus or minus S.D

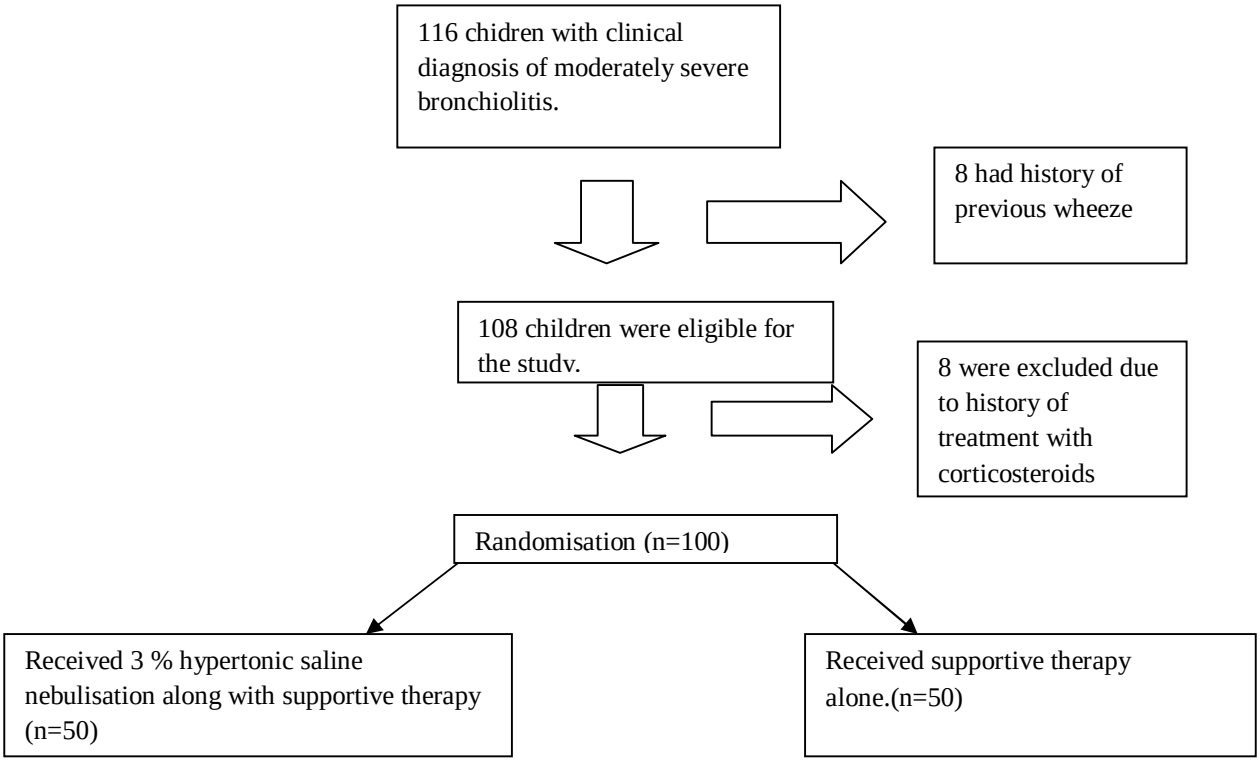
Categorical measurements were represented by percentage. Significance was assessed by five percent level of significance.

Statistical software:

For stastistical analysis SPSS version 16 is used

RESULTS

During the study 116 patients were admitted in to the study with a diagnosis of bronchiolitis with moderate severity. Of those 108 children were included 8 were not included due to previous history of wheeze. Amongst the 108 patients eight were excluded due to the prior treatment with corticosteroids.At last 100 children were analysed and randomization was done for them and they were randomized in to two groups of 50 each.The study group were administered 3% hypertonic saline nebulisation along with supportive care were 50 in number and the controls who received supportive care alone contained 50 children.

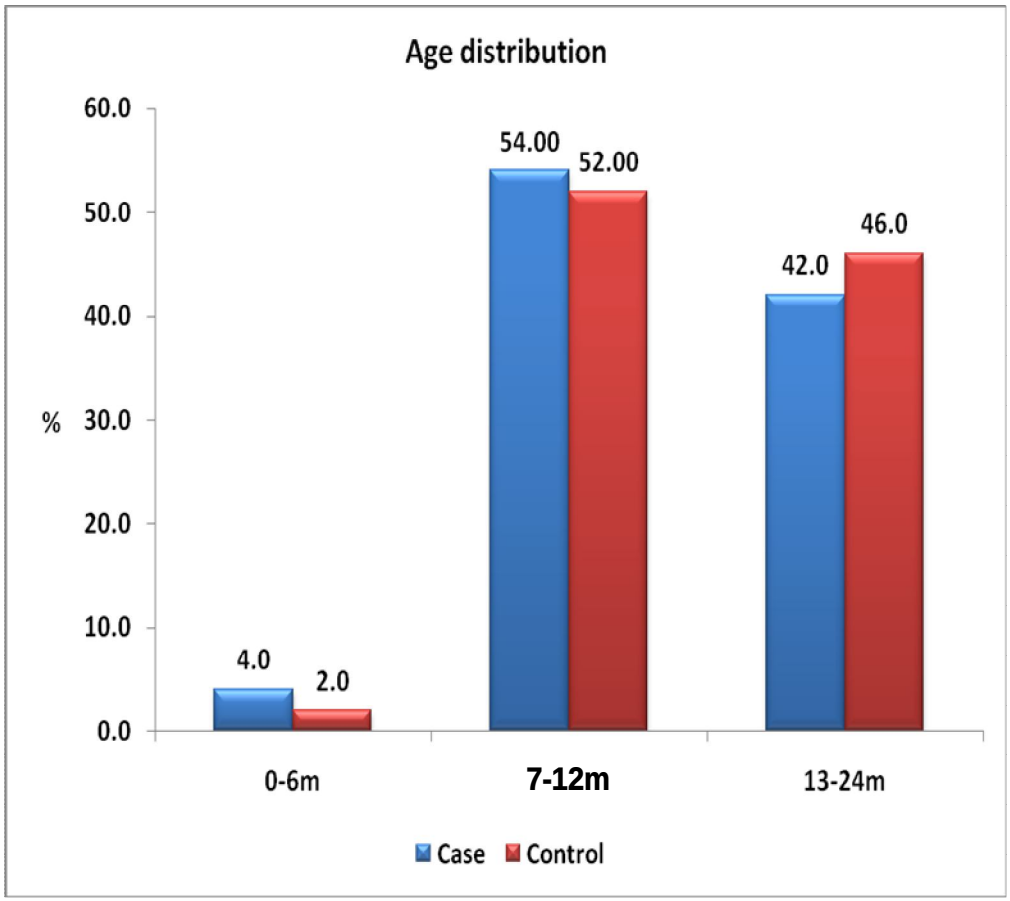


Supportive therapy included the administration of humidified oxygen and intravenous fluids.

POPULATION CHARACTERISTICS:

AGE DISTRIBUTION OF THE ENROLLED CHILDREN.

			Age			Total
			0-6m	7-12m	13-24m	
Group	Case	Count	2	27	21	50
		% within Group	4.0%	54.0%	42.0%	100.0%
	Control	Count	1	26	23	50
		% within Group	2.0%	52.0%	46.0%	100.0%
Total		Count	3	53	44	100
		% within Group	3.0%	53.0%	44.0%	100.0%



p value =0.801

In study done by us the age was comparable in the study and control groups.

The majority were were in the 7-12 month age group.

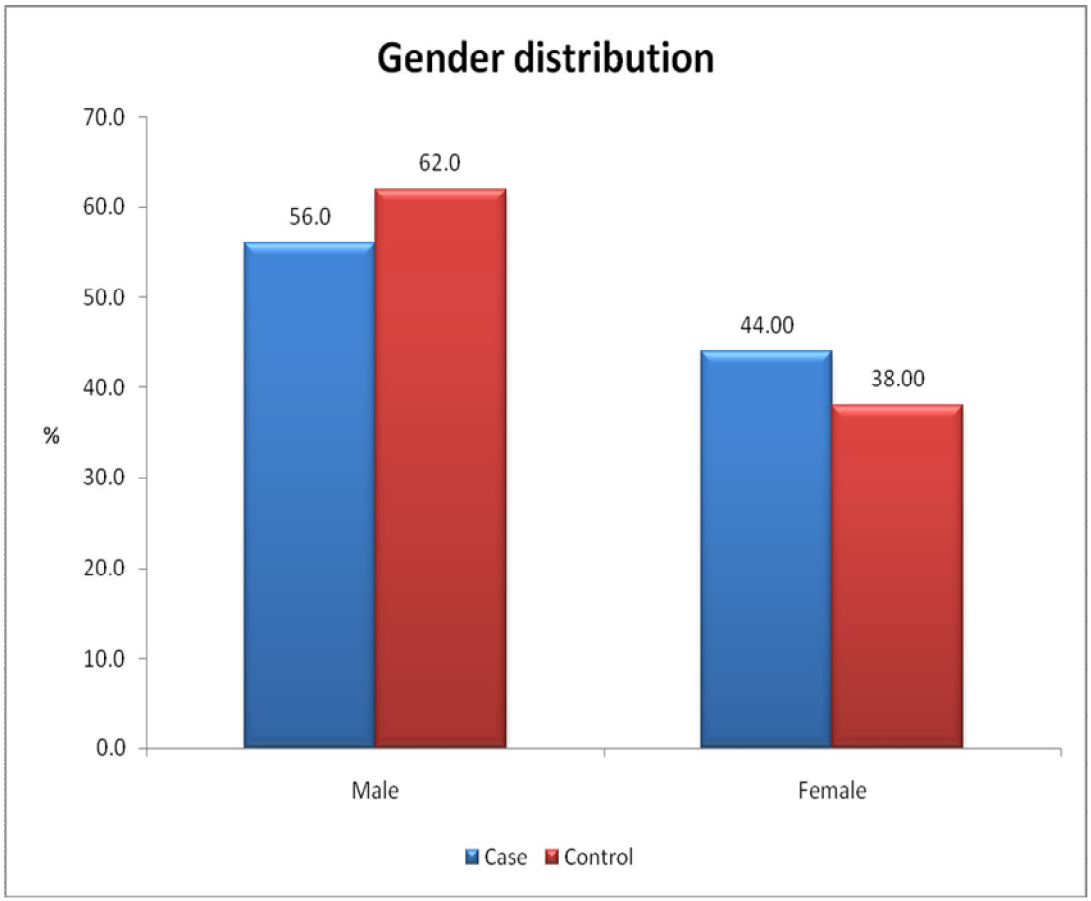
GENDER DISTRIBUTION:

		Sex		Total
		Male	Female	
Group	Case Count	28	22	50
	Case % within Group	56.0%	44.0%	100.0%
	Control Count	31	19	50
	Control % within Group	62.0%	38.0%	100.0%
	Total Count	59	41	100
	Total % within Group	59.0%	41.0%	100.0%

In this study males were more commonly affected than females.

The male to female ratio was 1.43:1

Male is to female ratios was comparable between the study group and the control group



P value = 0.542

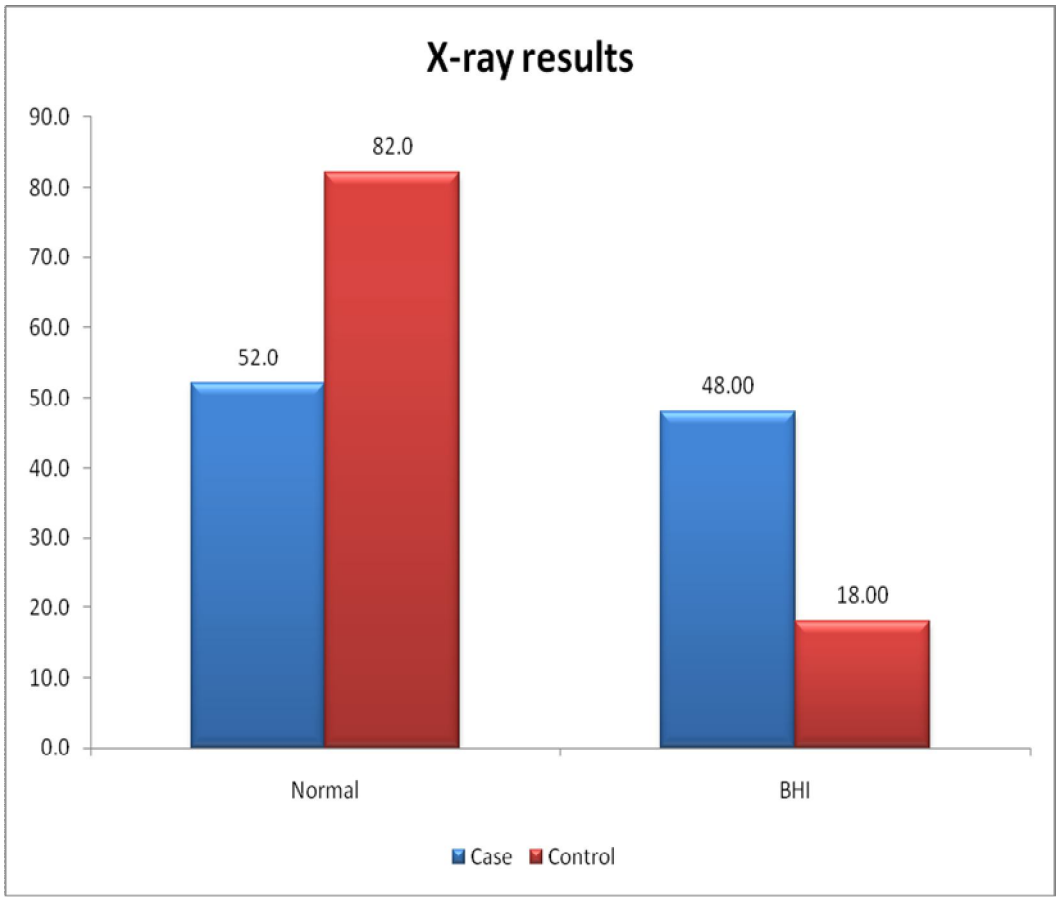
Amongst cases 56 % were males and remaining 40% were females.

Amongst controls 62 % were males and remaining 32 % were females.

CHEST X-RAY

			X_ray		Total
			Normal	BHI	
Group	Case	Count	26	24	50
		% within Group	52.0%	48.0%	100.0%
	Control	Count	41	9	50
		% within Group	82.0%	18.0%	100.0%
	Total	Count	67	33	100
		% within Group	67.0%	33.0%	100.0%

Amongst all cases clinically diagnosed as moderate bronchiolitis 67 % had normal X rays , only 33 % had the classical feature of bilateral hyperinflation.



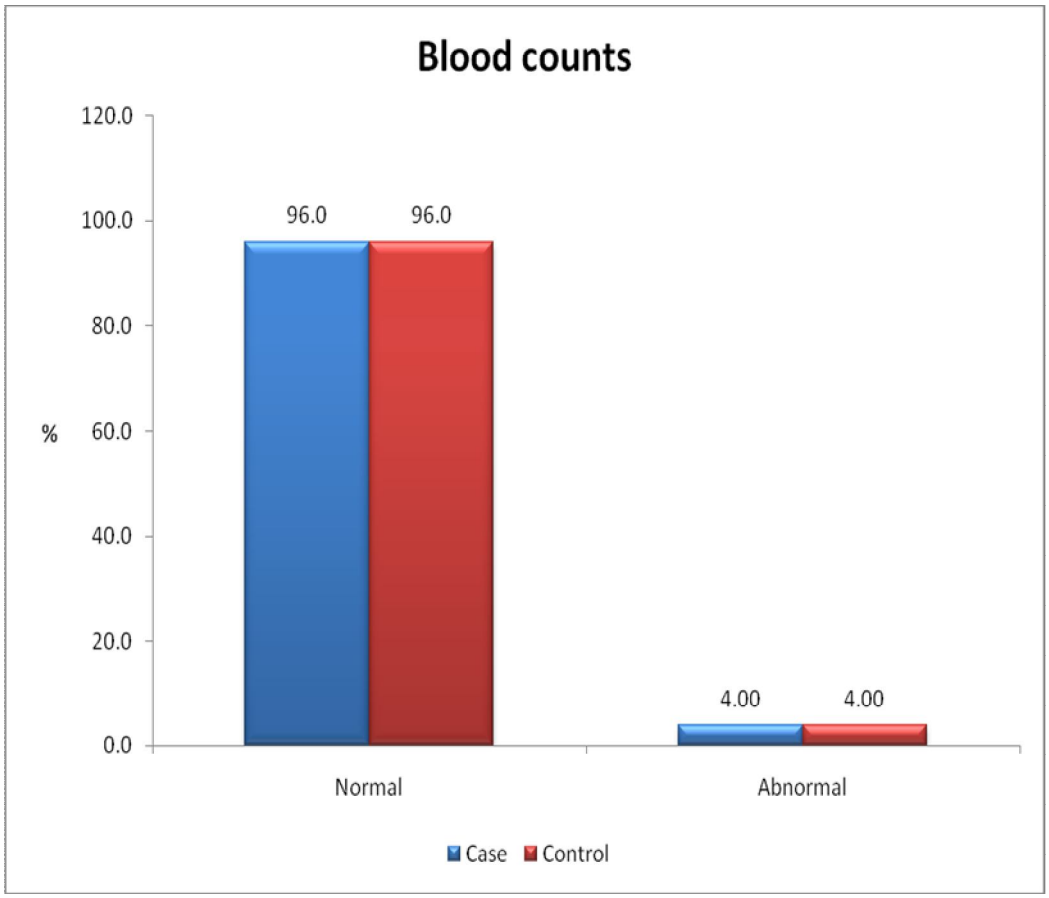
p value = 0.003

Amongst the study group there was a higher proportion of children with bilateral hyper inflation.

Hence the study group and the control group was not comparable with respect to bilateral hyper inflation in chest xray.

TOTAL BLOOD COUNT

			Blood_cnts		Total
			Normal	Abnormal	
Group	Case	Count	48	2	50
		% within Group	96.0%	4.0%	100.0%
	Control	Count	48	2	50
		% within Group	96.0%	4.0%	100.0%
Total		Count	96	4	100
		% within Group	96.0%	4.0%	100.0%



Amongst cases getting 3 % hypertonic saline nebulizations 4 percent had abnormal blood counts.

Similarly amongst controls receiving supportive therapy 4 percent had abnormal blood counts.

The two groups were comparable with regard to abnormal blood counts.

Only the upper and lower levels of age appropriate total leukocyte count was taken in to consideration.

HUMIDIFIED OXYGEN ADMINISTRATION

			O2	Total
			Yes	
Group	Case	Count	50	50
		% within Group	100.0%	100.0%
	Control	Count	50	50
		% within Group	100.0%	100.0%
Total		Count	100	100
		% within Group	100.0%	100.0%

Humidified oxygen was administered to all the cases in the study as well as in the control group as part of the supportive therapy.

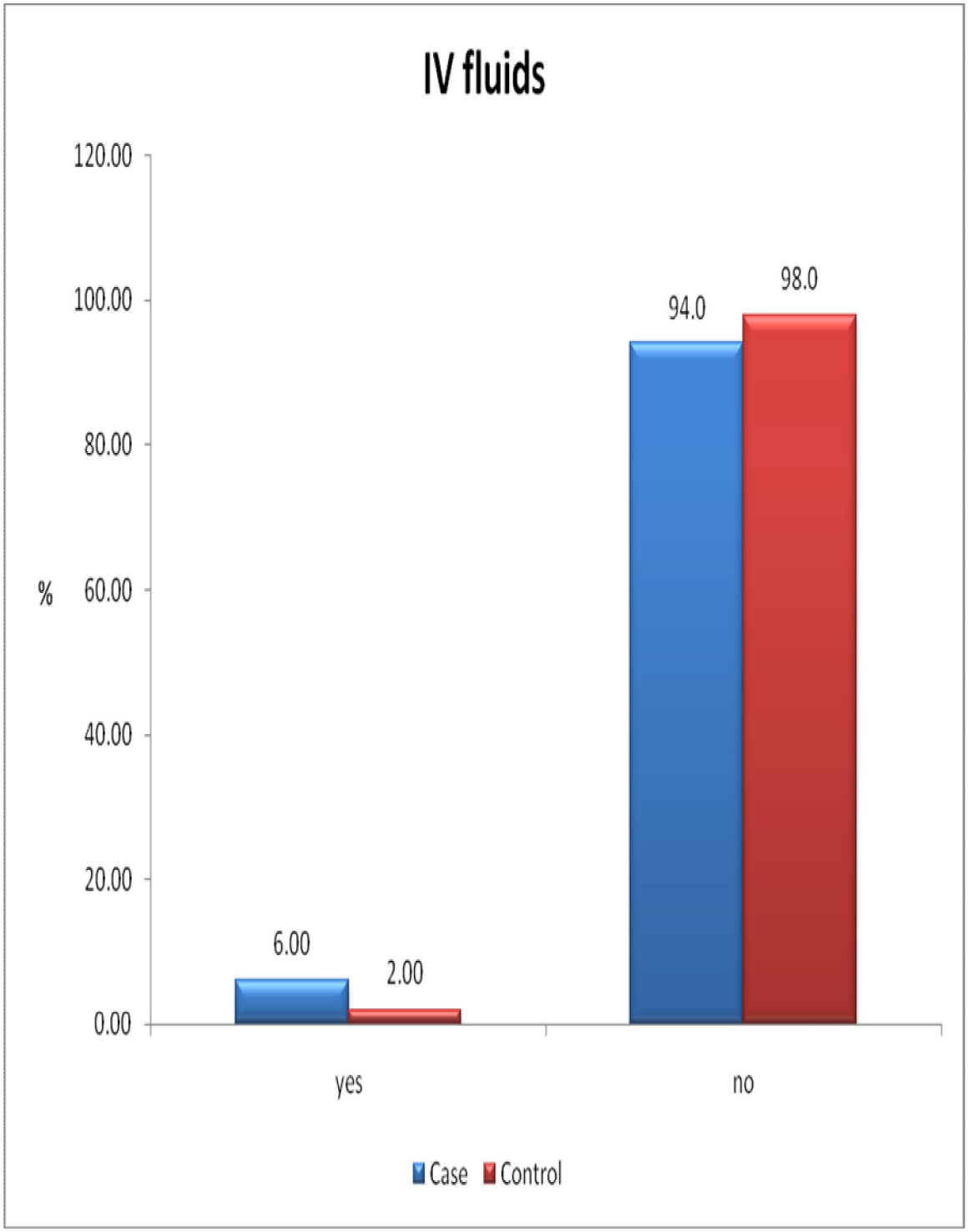
Hence the two groups were comparable with regard to oxygen administration.

ADMINISTRATION OF INTRAVENOUS FLUIDS.

			IV_fluids		
			No	Yes	Total
Group	Case	Count	47	3	50
		% within Group	94.0%	6.0%	100.0%
	Control	Count	49	1	50
		% within Group	98.0%	2.0%	100.0%
Total		Count	96	4	100
		% within Group	96.0%	4.0%	100.0%

Six percent of children in the group receiving hypertonic saline with supportive therapy required intravenous fluids.

Two percent of children receiving supportive therapy alone developed the need for intravenous fluids.


IV fluids
120.00
100.00
80.00
60.00
40.00
20.00
0.00
%
6.00
2.00
94.0
98.0
yes
no
Case
Control

P VALUE=0.617

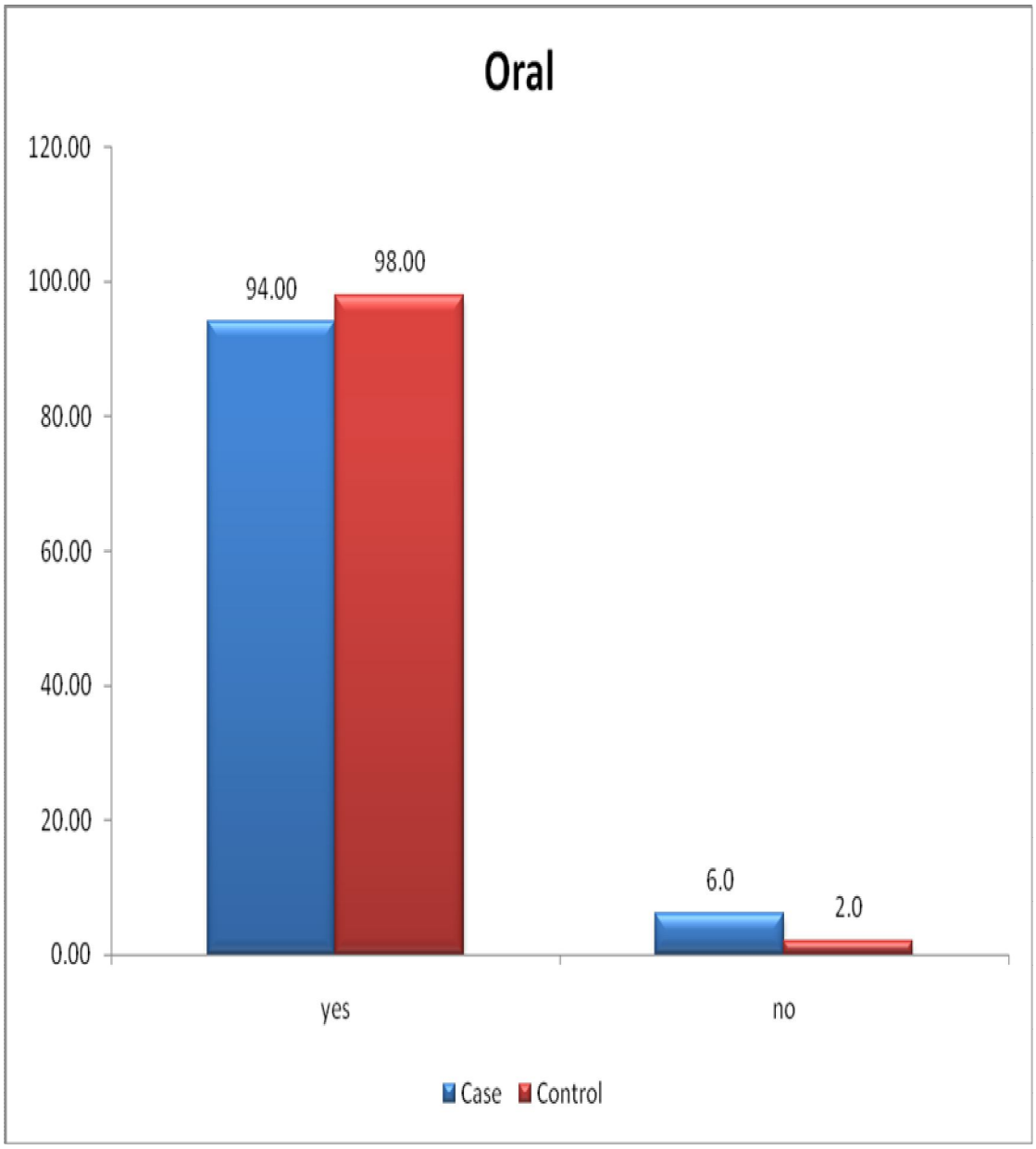
CHILDREN ON ORAL FEEDS

			Oral		Total
			Yes	No	
Group	Case	Count	47	3	50
		% within Group	94.0%	6.0%	100.0%
	Control	Count	49	1	50
		% within Group	98.0%	2.0%	100.0%
Total		Count	96	4	100
		% within Group	96.0%	4.0%	100.0%

94 % of the cases were able to take oral feeds in the group receiving hypertonic saline nebulisation.

98 % of the chidren receiving supportive therapy alone were able to take oral feeds

Overall 96 % of the children were able to take oral feeds and the remaining 4 % were given intravenous fluids.



ORAL FEEDS

P value = 0.617

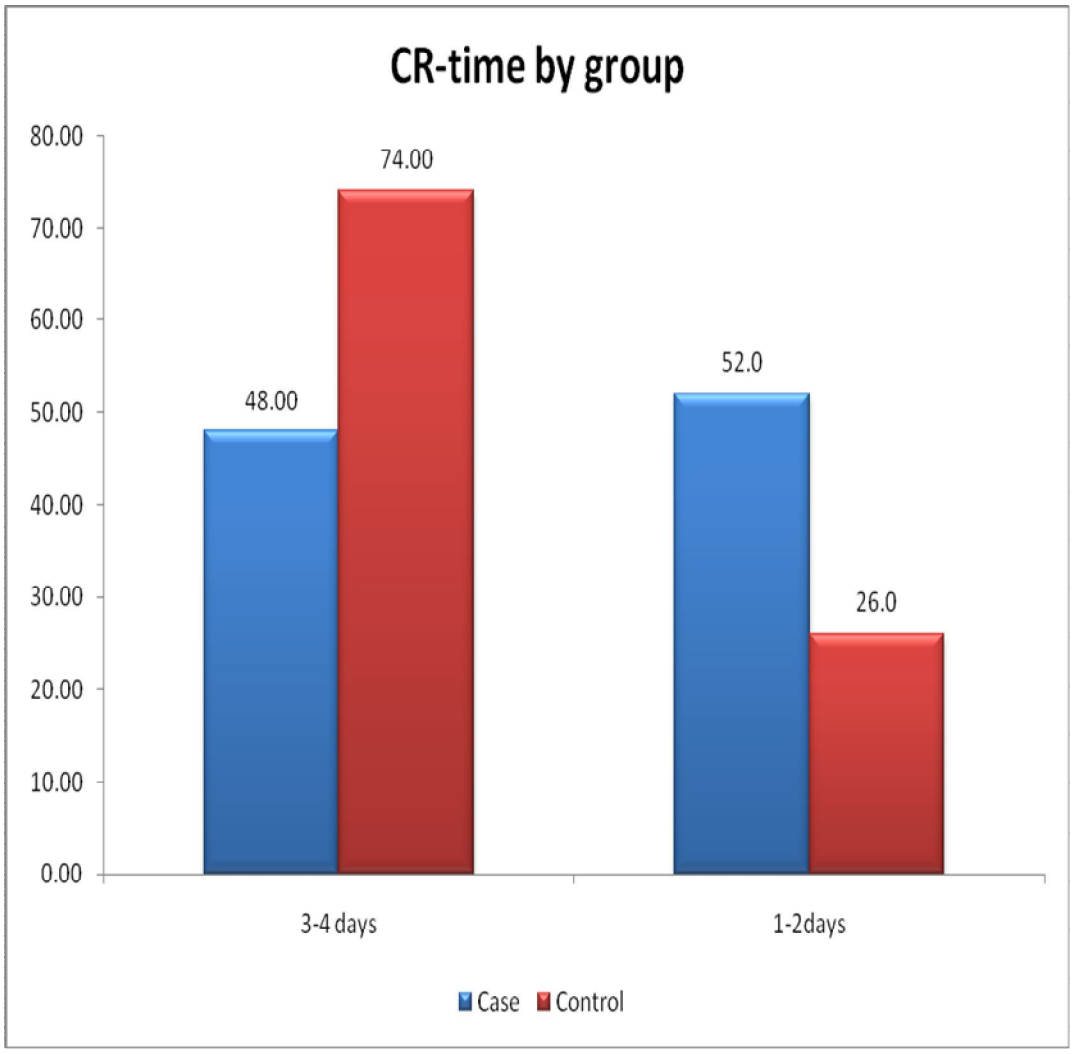
COUGH RESOLUTION TIME

			CR_time		Total
			3-4 days	1-2days	
Group	Case	Count	24	26	50
		% within Group	48.0%	52.0%	100.0%
	Control	Count	37	13	50
		% within Group	74.0%	26.0%	100.0%
Total		Count	61	39	100
		% within Group	61.0%	39.0%	100.0%

Amongst cases receiving 3 % hypertonic saline along with supportive therapy in 48 % of cases the cough got resolved in 3-4 days.In 52 % of the cases the cough got resolved in 1-2 days.

Amongst children receiving supportive therapy alone in 74 % of the cases the cough resolved in 3-4 days. In remaining 26 % the cough got resolved in 1-2 days.

Overall in both the groups, in 61 % of the cases the cough got resolved in 3-4 days. In 39 % of the cases the cough got resolved in 1-2 days



P value = 0.014 statistically significant

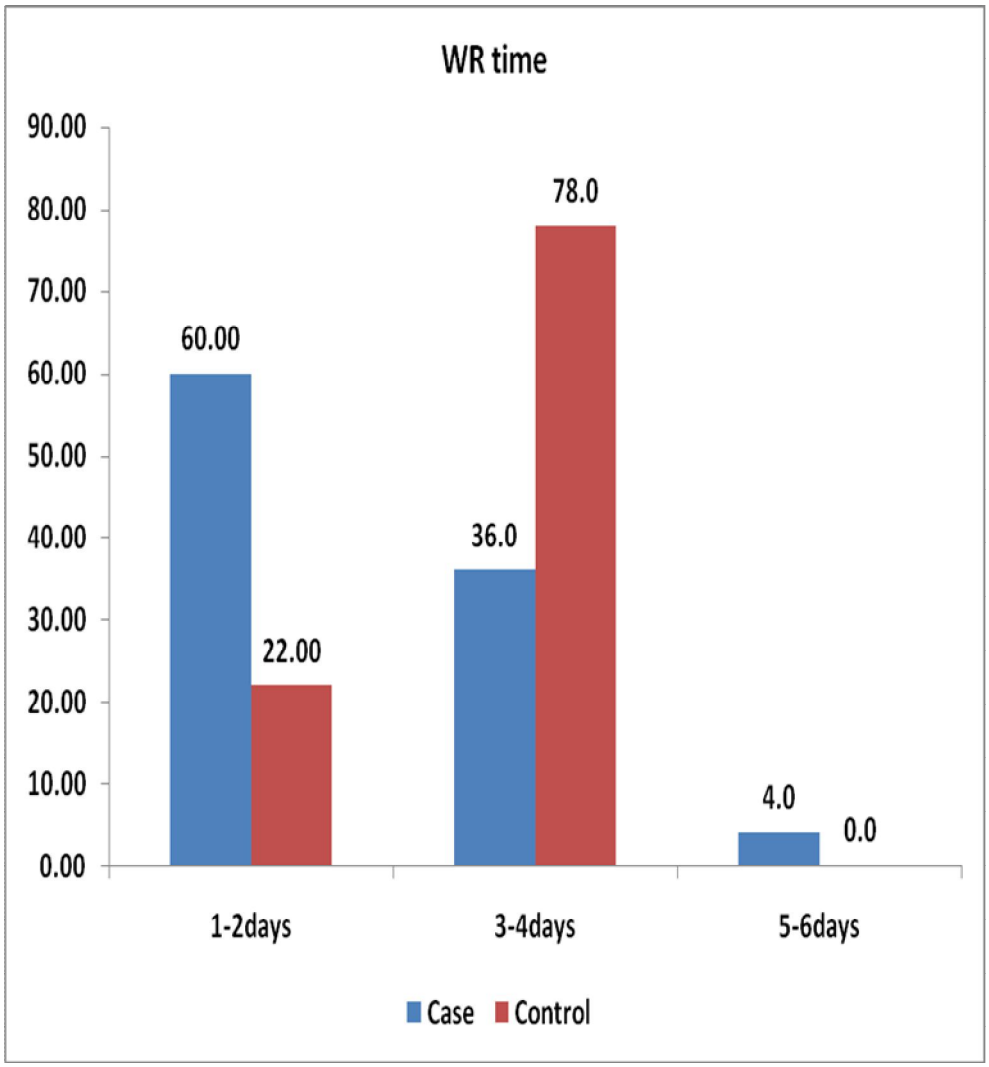
WHEEZE RESOLUTION TIME

			WR_time			Total
			1-2days	3-4days	5-6days	
Group	Case	Count	30	18	2	50
		% within Group	60.0%	36.0%	4.0%	100.0%
	Control	Count	11	39	0	50
		% within Group	22.0%	78.0%	.0%	100.0%
Total		Count	41	57	2	100
		% within Group	41.0%	57.0%	2.0%	100.0%

Amongst children receiving hypertonic saline along with supportive therapy in 60 % of cases the wheeze got resolved in 1-2 days. In 36 % of children the wheeze got resolved in 3-4 days. In remaining 4 % the wheeze got resolved in 5-6 days.

Amongst children receiving supportive therapy alone in 22 % of the cases the wheeze got resolved in 1-2 days. In 78 % of the cases the wheeze got resolved in 3-4 days.

Overall in 41 % of the cases the wheeze got resolved in 1-2 days. In 57 % of the cases the wheeze resolved in 3-4 days . In the remaining 2 % of the cases the wheeze got resolved in 5-6 days.



P value = 0.000

ADVERSE EFFECT:

			Adv_effect
			Nil
Group	Case	Count	50
		% within Group	100.0%

No adverse effects were observed in the group receiving 3 % hypertonic saline nebulisation along with supportive therapy. Supportive therapy included oxygen administration and IV fluids.

T-Test

LENGTH OF STAY:

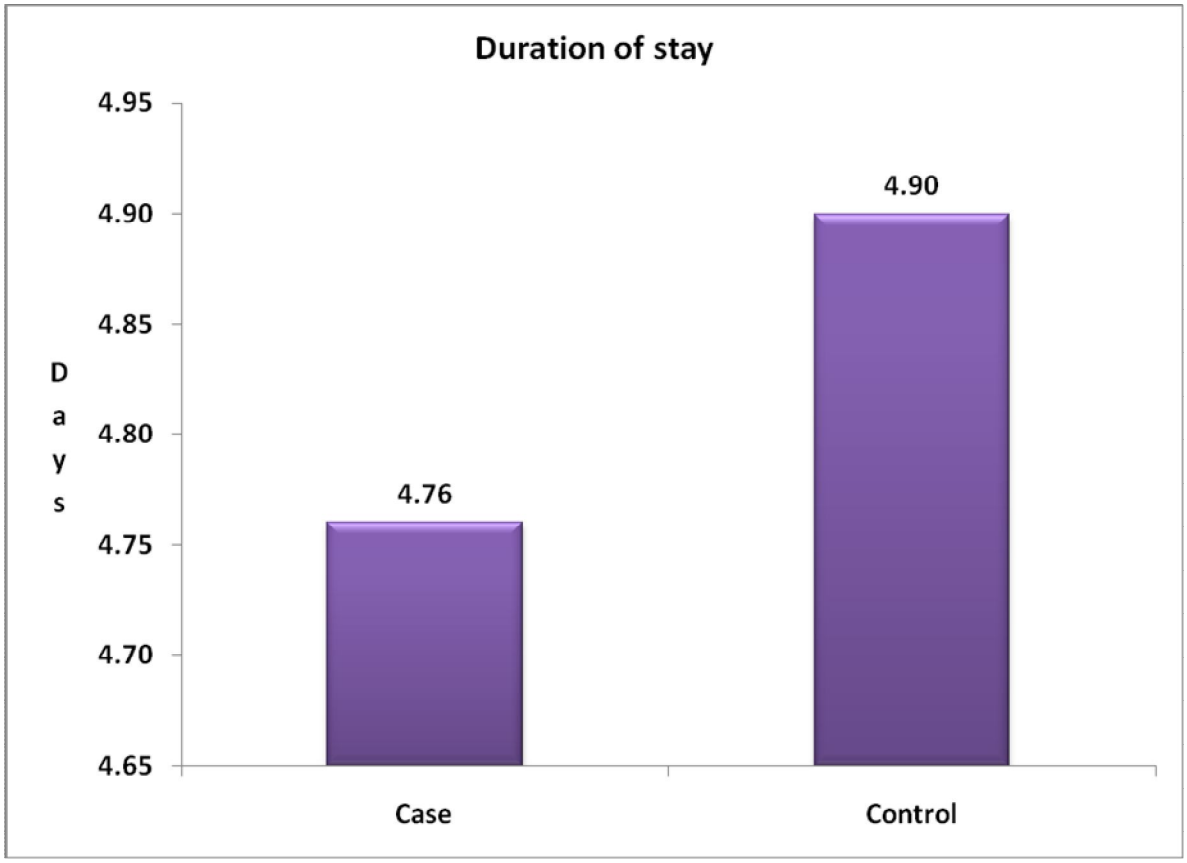
Group Statistics					
	Group	N	Mean	Std. Deviation	P-value
Dur_Stay	Case	50	4.76	.657	0.235
	Control	50	4.90	.505	

The mean duration in the group receiving 3 % hypertonic saline along with supportive therapy was found to be 4.76±0.567 days.

The mean duration in the group receiving supportive therapy alone was found to be 4.90±0.505 days.

However this was not found to be statistically significant.

P value = 0.235



P value = 0.235

The primary outcome parameter considered in this study was duration of hospital stay.

The secondary outcome parameters which were considered in this study was cough resolution time and wheeze resolution time.

The adverse effects were observed in the group receiving 3 % hypertonic saline nebulisation.

The mean duration of hospital stay in the group receiving 3 % hypertonic saline nebulisation along with supportve therapy was found to be 4.76±0.567 days.

The mean duration of hospital stay in the group receiving supportive therapy alone was found to be 4.90±0.505 days.

There was a 3.9 percentage reduction in length of stay in the hypertonic saline group compared to the control group which received supportive therapy alone.

But these findings were not statistically significant.

The cough resolution time was shorter in the 3 % hypertonic saline group compared to the controls receiving

supportive therapy alone.

The reduction in the cough resolution time was statistically significant.

The wheeze resolution time was also shorter in the group receiving 3% hypertonic saline along with supportive therapy as compared to the group receiving supportive therapy.

The difference in the wheeze resolution time was statistically significant.

There were no adverse effects observed in the group receiving 3 % hypertonic saline along with supportive therapy.

DISCUSSION

Bronchiolitis is a common cause of lower respiratory infection in the age group less than two years of age. Mostly it is due to a viral etiology. Usually it gets resolved spontaneously and respiratory syncytial virus is the commonest agent contributing to almost 50 % of the disease

A study was done in India[48] regarding the incidence and the pattern of infection and it was found to be the same as in any other part of the world. The disease has a peak incidence mainly during the months of september through january, but it can occur at any time of the year. In the study done in our hospital the incidence was maximum during the winter months but sporadic cases did occur through out the year.

This fact is supported by the study done by John tj et al[48] and yeleokar et al[49] who studied the seasonal pattern of the disease caused by respiratory syncytial virus.

Bronchiolitis usually affects young children and the disease is more severe when it occurs in infants less than six months of age. In our study all chidren less than two years were admitted (

range 0-24 months).

Children in the 6-12 months category constituted the majority in our study. They accounted for 53 % of the cases.This was in contrast to a cohort study done by Fjaerli et al regarding the incidence and risk factors in respiratory syncytial virus disease.

Bronchiolitis is more common in males compared to females. In or study too a male predominance was observed accounting for 59 % of all admissions. The male: female ratio in our study was found to be 1.43:1. This observation is consistent with the work done by John tj et al in south india. They studied the etiological factors, incidence , risk factor and clinical presentation of respiratory tract infection in children and came to the conclusion that males were more commonly affected than females. In their study the male is to female ratio was found to be 1.6:1.

Fjaerli et al[50] too did a similar study in Norway and came out with the finding that there was male predominance and the male is to female ratio was 1.42:1. Simoes EAF[51] in his study done in America studied the risk factors which lead to a severe RSV disease and came out with the findings that respiratory

syncytial virus infection was more common in boys than in girls and the ratio was 2:1. Also boys were found to be affected in a more severe manner compared to girls.

Bronchiolitis is mainly a clinical diagnosis and investigations are not necessary to diagnose the disease. And blood counts are usually not done. They are done if there is atypical presentation and also to rule out other causes.

In our study 4 % in the group receiving hypertonic saline along with supportive therapy and 4 % in the group receiving supportive therapy had abnormal total blood counts . In our study all children who had abnormal total blood counts had increased total leucocyte count when compared to age appropriate values and they were equally distributed in both the groups. The groups were comparable in this respect.

In Bronchiolitis there will usually be hyperinflation of lungs and atelectasis. In our study we found that majority of the x-rays were normal 67 % and in the remaining 33 % there was bilateral hyperinflation or flattening of diaphragm or prominence of retrosternal space or bulging of intercostal spaces or a combination

of these findings.

Our observations are in contrast to a study done by scuh et al who came out with the findings that majority of the cases of bronchiolitis had the radiological feature characteristic of bronchiolitis. The study was a follow up study and he studied the utility of chest x-ray to diagnose bronchioli.

In our study the primary outcome measured was the length of stay. The length of stay was arrived at by measuring the duration required to attain discharge criteria. The mean duration of length of stay in our hospital amongst the group receiving 3 % hypertonic saline and supportive therapy was 4.76±0.657.

This was in contrast to the study done by Mandelbeg et al[43] , Tal et al[44] , and Kuzik et al[45]. In the study done by Mandelber et al the mean duration of hospital stay was found to be 3.5. In the study done by Tal et al the mean duration of hospital stay was found to be 3.1. Similarly in a study done by kuzik et al the mean duration of hospital stay was found to be 3.1.

This difference in lengthof stay could be explained by the fact that in different centres the severity could have been different

as well as the role of inter observer variation in grading of severity cannot be underplayed.

In the 3 % hypertonic saline group the duration of stay was slightly lesser compared to the group which received supportive therapy alone. But this difference did not attain statistical significance.

By trying 3 % hypertonic saline we found that there was a 3.9 percentage reduction in length of stay in the group that received 3 % hypertonic saline along with supportive therapy compared to the group that received supportive therapy alone. However this was not statistically significant.

These findings are in contrast to studies done by Mandelberg et al[43] , kuzik et al[44] and Tal et al[45]. Taal et al arrived at a mean reduction of 0.9 days (26%)His findings were statistically significant.Kuzik et al observed a 26 % reduction in length of stay with the use of 3% hypertonic saline nebulisations.

Maandelberg et al[43] in his study usin 3 % hypertonic saline nebulisations in cases of mild and moderate bronchiolitis arrived at a finding of 1 day reduction in length of stay (25%) .The

difference in observations could be attributed to the fact that in our study only moderate cases of bronchiolitis were included.

The secondary outcomes measured in our study was cough resolution time. In our study the cough resolution time in the group receiving 3 % hypertonic saline along with supportive therapy was lesser than the controls receiving supportive therapy alone.

And this difference in cough resolution time between the two groups was statistically significant.

The other secondary outcome measured in our study was wheeze resolution time. The wheeze resolution time in the group receiving 3 % hypertonic saline group was lesser compared to the controls who received supportive therapy alone. And this finding was statistically significant.

In general the use of 3% hypertonic saline is considered to be fairly safe. Some studies conducted in patients suffering from cystic fibrosis have reported bronchospasm as an adverse effect. But lesser concentrations of hypertonic saline have been studied in bronchiolitis and found to be safe.

In our study no adverse effects were noted due to 3 % hyper

tonic saline administration. The same was observed in studies done by Mandelberg et al[43] ,kuzik et al[45] and Tal et al[44] .They did not observe any adverse effects in their use of 3 % hypertonic saline nebulisation.

STUDY LIMITATIONS

As we included only moderate cases of bronchiolitis , the role of hypertonic saline in severe bronchiolitis wherein other factors might play a role is unclear.

Since bronchiolitis is mainly a clinical diagnosis , the role of intraobserver variation cannot be underplayed.

Because of the small sample size a significant reduction in duration of hospital stay could not be ascertained.

SUMMARY

3 % hypertonic saline nebulization does not reduce the length of stay in cases of moderate bronchiolitis in a significant manner.

3 % Hypertonic saline nebulizations decrease the clinical severity by decreasing the cough resolution and wheeze resolution time in children admitted with moderate bronchiolitis. This was statistically significant.

3 % Hypertonic saline administration in children did not produce any adverse effects and it is safe to use in children diagnosed with bronchiolitis.

CONCLUSIONS

In conclusion our study suggests that 3 % hypertonic saline helps to reduce the cough resolution and wheeze resolution time thereby decreasing the clinical severity in hospitalized patients admitted with a diagnosis of moderately severe bronchiolitis.

Further studies are required to see if 3 % hypertonic saline has an effect on the length of stay.

3 % hypertonic saline was found to be safe in treating bronchiolitis in children.

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"EFFICACY OF 3% HYPERTONIC SALINE NEBULISATION IN CHILDREN HOSPITALIZED WITH MODERATE BRONCHIOLITIS"

1.	**Patient name (in Caps)**	**Sex** 1. Male ☐ 2. Female ☐
2.	**Age**	YY ☐☐ MM ☐☐
3.	**Date of admission** ☐☐ ☐☐ ☐☐	**Date of discharge** ☐☐ ☐☐ ☐☐
4.	**Father's Name**	**Qualification** : 1. Illiterate 2 .Primary (≤ grade 5) 3. Secondary (grade 5-12) 4. Graduate Occupation: 1. Unemployed 2. Unskilled labour 3. Skilled labour 4. Business 5. Professional 6. Others
5.	**Mother's Name**	**Qualification** : 1. Illiterate 2.Primary (≤ grade 5) 3. Secondary (grade 5-12) 4. Graduate ☐ Occupation: 1. Unemployed 2. Unskilled labour 3. Skilled labour 4. Business 5. Professional 6. Others ☐
6.	**Residence**	1. Chennai Corporation 2. Others ☐
7.	**Address** **Door No:** **Street :**	WD/Town State: Pin Code: ☐☐☐☐☐☐
8.	**Socio Economic Class Modified Kuppyswamy scale**	Specify--

CLINICAL HISTORY

9.	**Fever**	1. Yes ☐ 2. No ☐
	a. If Yes	Duration
	b. Amplitude	1.Low 2. Moderate 3. High
	c Periodicity	1.Continuous 2. Intermittent 3. Remittent
	d. Chillis	1. Yes 2. No ☐
10.	**Cough & Cold**	1.Yes ☐ 2. No ☐ Duration-----

11.	**H/O Breathlesness**	1.Yes ☐ 2. No ☐ Duration
12.	**H/O Cyanosis**	1.Yes ☐ 2. No ☐ Duration
13.	**H/O Chest retractions**	1.Yes ☐ 2. No ☐ Duration
14.	H/O Noisy Breathing	1.Yes ☐ 2. No ☐ Duration
15.	Refusal of feeds	1.Yes ☐ 2. No ☐ Duration
16.	H/O bad CRP	1.Yes ☐ 2. No ☐ If yes Specify a.Nasal blowing b.Oil instillation c.Sambrani fumes d.Others
17.	Skin Infections	1.Yes ☐ 2. No ☐
18.	Ear discharge	1.Yes ☐ 2. No ☐
19.	**H/O of Vomiting**	1.Yes ☐ 2. No ☐ Duration
20.	**Others Specify**	
21.	**Immunisation** **a. National immunization schedule**	1. Up to Age 2. Not upto age 3. Unimmunized 4. Not known
	b. Others Specify	

PAST HISTORY

22.	**H/O Measles**	**When –** **Treatment details**
23.	H/O of Hospitalisation	1.Yes ☐ 2. No ☐ Duration ---- Diagnosis
24.	H/O of seizures	1.Yes ☐ 2. No ☐ If Yes , No.of episodes /year---- Treatment details
25.	Developmental delay	1.Present 2.Absent

TREATMENT HISTORY

26.	**X-ray chest taken**	X-ray report – 1.
27.	Antibiotics	1. Yes 2. No

EXAMINATION

28.	**Weight -**	Height -		
29.	**Sensorium**	1. Normal	2. Altered	
30.	**Nutritional status (specify)**			
31.	**Pulse**	Rate-		
32.	**BP (mm of Hg)**			
33.	**RS**			
34.	**Respiratory Rate**	1. >40 2. >50 3. >63		
35.	**Work of Breathing**	1.Grunt	2. Stridor	3.Retractions
36.	Tracheal position	1.midline	2.Right	3.Left
		RIGHT	LEFT	AREAS
37.	**Breath sounds**			
38.	**If any other findings (specify)**			
39.	**CVS**	1. Normal	2. Abnormal	
	If any findings (specify)			
40.	**Abdomen**	1. Normal	2. Abnormal	
	If any findings (specify)			
41.	**CNS**	1. Normal	2. Abnormal	
42.	**If any findings (specify)**			

INVESTIGATIONS

	Blood Count		
43.	**Total Count**	Cells/cubic mm	
44.	**X ray Chest**	Date	Report
	I		
	II		

TREATMENT

45.	**Oral feeds started on**	
46.	**IV fluids**	1. Yes 2. No
47.	**f yes Specify**	
48.	**HUMIDIFIED OXYGEN ADMINISTRATION**	1. Yes 2. No
49.	**NEBULISED HYPER TONIC SALINE - 3% 8th hourly**	1. Yes 2. No

Crosstabs

Group * Age

Crosstab

			Age			
			0-6m	6-12m	13-24m	Total
Group	Case	Count	2	27	21	50
		% within Group	4.0%	54.0%	42.0%	100.0%
	Control	Count	1	26	23	50
		% within Group	2.0%	52.0%	46.0%	100.0%
Total		Count	3	53	44	100
		% within Group	3.0%	53.0%	44.0%	100.0%

P=0.801

Group * Sex

Crosstab

			Sex		
			Male	Female	Total
Group	Case	Count	28	22	50
		% within Group	56.0%	44.0%	100.0%
	Control	Count	31	19	50
		% within Group	62.0%	38.0%	100.0%
Total		Count	59	41	100
		% within Group	59.0%	41.0%	100.0%

P=0.542

Group * X_ray

Crosstab

			X_ray		
			Normal	BHI	Total
Group	Case	Count	26	24	50
		% within Group	52.0%	48.0%	100.0%
	Control	Count	41	9	50
		% within Group	82.0%	18.0%	100.0%
Total		Count	67	33	100
		% within Group	67.0%	33.0%	100.0%

P=0.003

Group * Blood_cnts

Crosstab

			Blood_cnts		
			Normal	Abnormal	Total
Group	Case	Count	48	2	50
		% within Group	96.0%	4.0%	100.0%
	Control	Count	48	2	50
		% within Group	96.0%	4.0%	100.0%
Total		Count	96	4	100
		% within Group	96.0%	4.0%	100.0%

P=1.000

Group * O2

Crosstab

			O2	
			Yes	Total
Group	Case	Count	50	50
		% within Group	100.0%	100.0%
	Control	Count	50	50
		% within Group	100.0%	100.0%
Total		Count	100	100
		% within Group	100.0%	100.0%

Group * IV_fluids

Crosstab

			IV_fluids		
			No	Yes	Total
Group	Case	Count	47	3	50
		% within Group	94.0%	6.0%	100.0%
	Control	Count	49	1	50
		% within Group	98.0%	2.0%	100.0%
Total		Count	96	4	100
		% within Group	96.0%	4.0%	100.0%

P=0.617

Group * Oral

Crosstab

			Oral		
			Yes	No	Total
Group	Case	Count	47	3	50
		% within Group	94.0%	6.0%	100.0%
	Control	Count	49	1	50
		% within Group	98.0%	2.0%	100.0%
Total		Count	96	4	100
		% within Group	96.0%	4.0%	100.0%

P=0.617

Group * CR_time

Crosstab

			CR_time		
			3-4 days	1-2days	Total
Group	Case	Count	24	26	50
		% within Group	48.0%	52.0%	100.0%
	Control	Count	37	13	50
		% within Group	74.0%	26.0%	100.0%
Total		Count	61	39	100
		% within Group	61.0%	39.0%	100.0%

P=0.014

Group * WR_time

Crosstab

			WR_time			
			1-2days	3-4days	5-6days	Total
Group	Case	Count	30	18	2	50
		% within Group	60.0%	36.0%	4.0%	100.0%
	Control	Count	11	39	0	50
		% within Group	22.0%	78.0%	.0%	100.0%
Total		Count	41	57	2	100
		% within Group	41.0%	57.0%	2.0%	100.0%

P=0.000

Group * Adv_effect

Crosstab

			Adv_effect	
			Nil	Total
Group	Case	Count	50	50
		% within Group	100.0%	100.0%
	Control	Count	50	50
		% within Group	100.0%	100.0%
Total		Count	100	100
		% within Group	100.0%	100.0%

T-Test

[DataSet1]

Group Statistics

	Group	N	Mean	Std. Deviation	P-value
dur_stay	Case	50	4.76	.657	0.235
	Control	50	4.90	.505	